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Assistant Commissioner for Patents, Washington, D.C. 20231.


Tamara Alcaraz

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Nahum SONENBERG et al.

Serial No.: To Be Assigned

Filing Date: Herewith

For: NON-HUMAN TRANSGENIC ANIMAL
WHOSE GERM CELLS AND SOMATIC
CELLS CONTAIN A KNOCKOUT
MUTATION IN DNA ENCODING 4E-
BP1

Examiner: To Be Assigned

Group Art Unit: To Be Assigned

PRELIMINARY AMENDMENT

Box PATENT APPLICATION
Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Prior to examination of the above-captioned application, please enter the following
amendments.

AMENDMENTS

In the Specification:

Please insert the following paragraph starting on page 1 at line 5

CROSS-REFERENCE TO RELATED APPLICATIONS

The present application claims priority to PCT/CA00/00388 filed April 7, 2000 which claims priority to provisional application nos. 60/128,559 filed April 9, 1999 and 60/179,743 filed February 2, 2000, all of which are hereby incorporated in their entirety by reference.

In the Claims:

Please amend the following claims.

13. (Amended) The method of claim 12, wherein said eIF-4E sequestering agent comprises a sequence having an amino acid sequence selected from YxxxxL ϕ , Yx+xf $\phi\phi$, + ϕ xYx+xf $\phi\phi$, + $\phi\phi$ Y-+xF/A $\phi\phi$ xxRxSP, and + $\phi\phi$ Y-+xfL ϕ xxRxSP, or + ϕ xYx+xfL ϕ xxxxxx wherein + and - refer to a charged amino acid; ϕ is a hydrophobic amino acid; x is any amino acid; and the capital letters refer to the known one letter code for amino acids.

17. (Amended) A method of identifying an agent which modulates glucose and/or fat metabolism *in vivo* comprising:

- a) providing a translationally active preparation of translation factors and at least one mRNA having a cap structure whose translation is cap-dependent;
- b) measuring the initiation of translation on said mRNA, or the binding of at least some translation factors of a) to said cap of said mRNA in the presence and in the absence of an agent suspected of modulating the translation efficiency of cap-dependent mRNAs or the binding of translation factors to the cap structure thereof, thereby identifying an agent which modulates cap-dependent translation and wherein a difference in the translation activity and/or binding in the presence of the agent, as compared to that in the absence thereof identifies said agent as a modulator of cap-dependent translation;
- c) administering said agent identified in b) to an animal; and

d) measuring glucose and/or lipid levels in the animal of step c) and comparing same with that of a control animal, not having been administered said agent, wherein a difference in glucose and/or lipid levels of the animal of step c) as compared to that of the control animal identifies said agent as a modulator of glucose or fat metabolism *in vivo*.

21. (Amended) A modulator of glucose or fat metabolism *in vivo* identified by the method of claim 17.

31. (Amended) A modulator of glucose or fat metabolism *in vivo* identified by the method of claim 28.

38. (Amended) A modulator of glucose and/or fat metabolism *in vivo* identified by the method of claim 7.

REMARKS

Claims 13, 17, 21, 31 and 38 have been amended. The amendments to the claims have been made to remove multiple dependency and reduce filing fees. These amendments are not intended to abandon, disclaim or dedicate any subject matter. The above amendment to the specification has been made to incorporate cross-reference to related applications.

Accordingly, Applicants submit no new matter by these amendments.

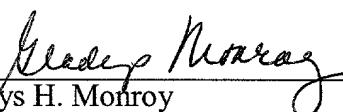
Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made**".

In the unlikely event that the fee transmittal is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 514012000400.

Respectfully submitted,

Dated: October 7, 2001

By:



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Please insert the following paragraph starting on page 1 at line 5

CROSS-REFERENCE TO RELATED APPLICATIONS

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In the Claims:

13. (Amended) The method of claim 12, wherein said eIF-4E sequestering agent comprises a sequence having an amino acid sequence selected from YxxxxL ϕ , Yx+xf $\phi\phi$, + ϕ xYx+xf $\phi\phi$, + $\phi\phi$ Y-+xF/A $\phi\phi$ xxRxSP, and + $\phi\phi$ Y-+xfL ϕ xxRxSP, or + ϕ xYx+xfL ϕ xxxxxx wherein + and - refer to a charged amino acid; ϕ is a hydrophobic amino acid; x is any amino acid; and the capital letters refer to the known one letter code for amino acids.

17. (Amended) [Method]A method of identifying an agent which modulates glucose and/or fat metabolism *in vivo* comprising:

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- c) administering said agent identified in b) to an animal; and

d) measuring glucose and/or lipid levels in the animal of step c) and comparing same with that of a control animal, not having been administered said agent, wherein a difference in glucose and/or lipid levels of the animal of step c) as compared to that of the control animal identifies said agent as a modulator of glucose or fat metabolism *in vivo*.

21. A modulator of glucose or fat metabolism *in vivo* identified by [any one of] the method[s] of claim[s] 17[, 18, 19 or 20].

31. A modulator of glucose or fat metabolism *in vivo* identified by [any one of] the method[s] of claim[s] 28[, 29, 30 or 31].

38. A modulator of glucose and/or fat metabolism *in vivo* identified by [any one of] the method[s] of claim[s] 7[, 17, 22, 27, 34, 35 or 36].